REMARKS

After entry of the instant Amendment, claims 1-9 and 11-13 are pending in the application. Claim 1 is amended while claims 10 and 14-18 are cancelled herein.

Claim Amendment:

Claim 1 is herein amended to remove the two distinct chemical structures that further defined the silicone polyether silicone. Accordingly, no new matter is added.

Pending Claim Objections:

The Examiner objects to claim 1 because two distinct chemical structures are recited in the claim (pre-amendment) but only one was given a roman numeral label. The amendment of claim 1 renders this objection moot such that the objection should be withdrawn.

The Examiner also objects to claim 12 because the previous status identifier "Currently Amended" was incorrect. The Applicant has corrected this typographical error in the claims set forth above and has properly indicated that claim 12, was then and currently remains, "Original." Accordingly, this objection is also now moot and should be withdrawn.

Pending Claim Rejections:

35 U.S.C. §112 ¶1:

The Examiner rejects claims 1-11 as failing to comply with the written description requirement because the previously amended claims introduced "new matter" into the claims. More specifically, the Examiner rejects claims 1-11 because the silicone polyether was amended such that it was selected from two particular chemical structures. As described above, the Applicant herein amends claim 1 such that the two particular chemical structures are no longer present. Accordingly, these rejections are now moot and should be withdrawn.

35 U.S.C. §112 ¶2:

The Examiner maintains the previously pending rejection of claim 10 as being indefinite due to the recitation of the phrase "less than about 20." The Applicant herein cancels claim 10 such that this rejection is moot and should be withdrawn.

35 U.S.C. §103:

I. The Examiner rejects claims 1-5, 7, 8, 10, 12, and 13 as obvious over U.S. Pat. No. 5,607,721 (the '721 patent to Ulman) in view of U.S. Pat. No. 6,121,373 (the '373 patent to Starch) and U.S. Pat. No. 5,785,978 (the '978 patent to Porter).

II. The Examiner also maintains the previous pending obviousness rejections of claims 12 and 13 over the '721 patent to Ulman in view of the '978 patent to Porter.

III. Moreover, the Examiner rejects claims 6, 9, and 11 as obvious over the '721 patent in view of the '373 patent and the '978 patent and further in view of U.S. Pat. No. 6,337,086 (the '086 patent to Kanios).

Relative to all three obviousness rejections (I)-(III) above, the Examiner asserts that the '721 patent discloses a (pressure sensitive) adhesive comprising a surfactant, such as a siloxylated polyether, and a bioactive agent, and methods of forming the same. However, in at least paragraph 6 on page 14 of the pending Office Action, the Examiner openly admits that the '721 patent is deficient because it "does not explicitly define at what state of mixing that the bioactive agent is added." Said differently, the '721 patent does not disclose, teach, or suggest the heart of this invention. This deficiency, as described in greater detail below, causes all of the obviousness rejections (I), (II), and (III) to fail.

No Prima Facie Case of Obviousness:

To overcome the deficiency of the '721 patent in both obviousness rejections (I) and (II)

above, the Examiner asserts that "forming a first composition comprising a hydrophilic drug or excipient and the silicone polyether is one of only *a small number of possibilities* for the additional order of the components" (emphasis added). Said differently, the Examiner asserts that there are only a few possible ways to combine components such that it would be obvious to experiment with each way in order to arrive at this invention. In using this reasoning, the Examiner is clearly relying on the "obvious to try" obviousness rationale outlined in MPEP §2141(III)(E) and concluding that, even though the art does not suggest any particular order of combination, it would be "obvious to try" the small number of possible combinations and arrive at the instant method. Although the Supreme Court in *KSR* approved of this type of rationale, its application must be carefully tailored and applied. As just one example, and as specifically cautioned by the CAFC in *In re O'Farrell*[1], it is *improper* to suggest that that an invention would have been obvious to try if the person of skill in the art would have had to vary all the parameters or try each of numerous possible choices until he arrived at a successful result where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.

In the instant case, the Applicant respectfully disagrees with the Examiner that that are only a small number of possibilities to consider when combining components. In fact, when even focusing on just the '721 patent by itself, there are many parameters to be considered, only some of which are as follows:

(1) Selection of a siloxylated polyether wax itself from the '721 patent that has the physical properties (such as melting point and viscosity) that would allow for successful combination with a solid powdered hydrophilic drug;

(2) Selection of temperature of combination, as it relates to the typically solid

[1] *In re O'Farrell*, 853 F.2d 894 (Fed. Cir. 1988)

siloxylated polyether wax of the '721 patent,[2] such that the wax and the solid powdered hydrophilic drug are miscible and can be successfully combined;

(3) Balancing the hydrophilicity and hydrophobicity of the end groups on the siloxylated polyether wax to balance hydrophilicity of the wax with the hydrophilicity of the solid powdered hydrophilic drug to ensure successful mixing[3];

(4) Selection of antioxidants, pigments, stabilizers, and fillers to include that may affect the combination of the solid powdered hydrophilic drug and the siloxylated polyether wax;[4]

(5) Balancing the hydrophilicity and hydrophobicity of the hot-melt silicone pressure sensitive adhesive of the '721 patent to balance hydrophilicity of the siloxylated polyether wax with the hydrophilicity of the solid powdered hydrophilic drug to ensure successful mixing[5];

(6) Selection of whether to combine the solid powdered hydrophilic drug with into the hot-melt silicone pressure sensitive adhesive directly or through one of "several" other modes[6];

and perhaps most importantly

(7) Selection of whether to combine the solid powdered hydrophilic drug with the siloxylated polyether wax before combination of the wax and the hot-melt silicone pressure sensitive adhesive.

Furthermore, the Examiner himself admitted on the record that the '721 patent "does not explicitly define at what state of mixing that the bioactive agent is added." In other words, the Examiner himself admits that the '721 patent gives no indication of which parameters are critical

[2] See Col. 5, Lines 56-63
[3] See Col. 5, Lines 12-55
[4] See Col. 4, Line 49-59 of the '721 patent; See also Col. 6, Lines 7-14 of the '721 patent
[5] See Col. 2, Line 57 to Col. 3, Line 9 of the '721 patent; See also Col. 3, Lines 27-43 of the '721 patent
[6] See Col. 7, Lines 11-38 and particularly Lines 15-17 of the '721 patent

or no direction as to which of many possible choices is likely to be successful. This lack of indication and direction in the '721 patent, in combination with the numerous parameters described above, show that it would not be at all obvious to arrive at the instant invention. Accordingly, the Applicant respectfully submits that the Examiner has not properly established a *prima facie* case of obviousness and should withdraw all obviousness rejections.

Unexpected Results:

In the alternative, and purely for the sake of argument, even if the Examiner had established a *prima facie* case of obviousness, the Supplemental Declaration filed concurrent herewith clearly describes both superior and, more importantly, entirely unexpected results using the method of this invention as compared to the prior art.

The Supplemental Declaration is executed by a Declarant of high skill in the art of developing adhesives for transdermal drug delivery. The Declarant describes and explains, in great detail, (1) the problems with the prior art and related technology, (2) the specific order of the method steps of the invention and what superior and unexpected results these method steps achieve, (3) the experimental data supporting the superior and unexpected results related to particle size and more precise drug delivery, (4) why smaller drug particles are more desirable and unexpected, and (5) why less variable drug release is desirable and unexpected. In other words, the Declarant not only describes the results associated with this invention but also describes the background against which the results can be properly evaluated and clearly shows why, when compared against that background, the results are both superior and unexpected.

The method of this invention includes a series of *sequential* steps set forth in both claims 1 and 12 which produce the superior and unexpected results of this invention.

(1) The first step involves forming the semi-solid composition containing the solid

powdered hydrophilic drug or the solid powdered hydrophilic excipient and the surfactant (e.g. a silicone polyether). Said differently, the surfactant and the drug/excipient are combined with each other independently from any other method steps and apart from the adhesive.

(2) The second step involves combining the adhesive (e.g. a silicone pressure sensitive adhesive), or a solution containing a solvent and the adhesive, and the semi-solid composition formed in (1) the first step.

(3) The third step involves mixing the semi-solid composition and the adhesive or the solution containing the solvent and the adhesive to form the adhesive matrix.

In short, using the sequential method steps of this invention (i) produces smaller hydrophilic drug particles in the adhesive matrices and (ii) minimizes agglomeration and crystal formation of the hydrophilic drugs which (iii) promote more predictable, more well-controlled, more precise, and less variable drug release from the adhesive matrices.

In accordance with the above, it is well established CAFC precedent that any experiments used to rebut *prima facie* obviousness need to show that results are not only superior but unexpected.[7] The results and data set forth in the Declaration are compared both qualitatively and quantitatively to comparative examples wherein the method steps of this invention are utilized in non-sequential order. The data shows that when the method steps of this invention are used "out of order," then the small hydrophilic drug particles are not formed, the drug particles agglomerate, cake, and form crystals, and that the drug release from the adhesive matrices is uncontrolled, highly variable, and unpredictable. In view of these comparisons, it is clear that the results associated with the sequential method steps of this invention are superior to those achieved in comparative examples.

[7] See *In re* Geisler, 116 F.3d 1465 (Fed. Cir. 1997).

In addition, these results are entirely unexpected from the perspective of one of skill in the art. As described in the Declaration, it is expected that the hydrophilic drug utilized in the method of the comparative example would disperse more effectively, quickly, and completely when added to a mixture of the PSA and the silicone polyether because the PSA includes 40 wt% of solvent. It is also expected that the mixture of the PSA and the silicone polyether would more efficiently coat the drug particles due to the hydrophilicity of the drug and the corresponding polarity of the mixture of the PSA and the silicone polyether. It is further expected that the entire matrix of the PSA would be made more hydrophilic through addition of the silicone polyether thereby improving the probability of the hydrophilic drug being more adequately dispersed throughout the entire matrix. In view of the above, it is therefore expected that the comparative examples would produce smaller drug particles that exhibit less agglomeration and caking and would accordingly exhibit more controlled, predictable, and precise drug release. However, this is not the case. In fact, just the opposite is true. As described above and in detail in the Declaration, using the sequential method steps of this invention (i) produces smaller hydrophilic drug particles in the adhesive matrices and (ii) minimizes agglomeration and crystal formation of the hydrophilic drugs which (iii) promote more predictable, more well-controlled, more precise, and less variable drug release from the adhesive matrices. For the aforementioned reasons, the data and results associated with the sequential method steps of this invention are unexpected.

Moreover, the CAFC also particularly points out that "'When an applicant demonstrates substantially improved results…and states that the results were unexpected, this should suffice to establish unexpected results in the absence of evidence to the contrary."[8] In so doing, the CAFC

[8] See *In re* Geisler, 116 F.3d 1465 (Fed. Cir. 1997). at 1471 citing In re Soni, 54 F.3d 746, 751 (Fed. Cir. 1995).

makes it very clear that when the results set forth by the Applicant are described as "superior" and "unexpected," these results should be accepted by the Office unless the Examiner convincingly demonstrates why, *in direct rebuttal to the opinion of one of high skill in the art*, the results are only superior and not unexpected. In this case, the Declarant attests to, and demonstrates, both how and why the results are both superior and unexpected. Thus, the Applicant respectfully submits that the Office should accept the superior and unexpected results attested to by the Declarant and withdraw all obviousness rejections.

Double Patenting Rejections:

The Examiner non-provisionally rejects claims 1-13 under the judicially created doctrine of obviousness-type double patenting over U.S. Pat. No. 5,607,721 (the '721 patent to Ulman) in view of U.S. Pat. No. 5,785,978 (the '978 patent to Porter) and U.S. Pat. No. 6,121,373 (the '373 patent to Starch). As described in great detail above, the Applicant respectfully disagrees with the Examiner regarding the §103 obviousness of these claims over the same references. In so doing, the Applicant hereby reasserts the aforementioned arguments, remarks, and explanation and respectfully submits that the double patenting rejection of claims 1-13 is improper and should be withdrawn.

Conclusion:

As set forth above, the Applicant has either overcome or traversed all pending objections and rejections. More specifically, it is clear that the Examiner has not properly established a *prima facie* case of obviousness to reject the pending claims. Nevertheless, the Applicant still submits superior and unexpected results that further demonstrate that this invention is non-obvious over the prior art. Accordingly, the Applicant respectfully requests that all objections and rejections be withdrawn and that a Notice of Allowance be promptly issued.

Although no fees are believed due, the Commissioner is authorized to charge our Deposit Account No. 08-2789 in the name of Howard & Howard Attorneys PLLC for any fees due or credit the account for any overpayment.

Respectfully submitted,

HOWARD & HOWARD ATTORNEYS PLLC

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/David M. LaPrairie/

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